Amendments to the Specification

Please replace the paragraph beginning at page 3, line 4, with the following amended paragraph.

Extensive work has been done characterizing the genes and expressed proteins for the alpha and beta subunits of TSH for various species. The alpha and beta subunits are synthesized from separate mRNAs coded by DNA from genes on separate chromosomes. For example, a single gene coding for the alpha subunit of TSH has been isolated and cloned from numerous species including humans (Fiddes, J, Goodman, H.M., Nature, 281, 351 (1979)), cattle (Erwin et al., Biochemistry, 22, 4856 (1983)), rat (Godine et al., J. Biol. Chem., 257, 8368 (1982)), mouse (Chin et al., Proc. Natl. Acad. Sci. USA, 78, 5329 (1981)), horse (M, O., Headon, D., Biochem. Soc. Trans., 3, 347S (1995)), and dog (Yang et al., Domestic Animal Endocrinology, 18, 379 (2000) ~~Yang et al., Domestic Animal Endocrinology, 18, 379 (2003)~~). This work has shown that there are two N-linked oligosaccharide chains attached to Asn56 and Asn82 and five intramolecular disulphide bonds in the α-subunit. A 24 amino acid leader sequence, which is cleared prior to secretion, is followed by a 96 amino acid mature protein in all species except the man, where the TSH α–subunit is a 92 amino acid mature protein (Gharib et al., Endocrine Reviews, 11, 177 (1990)).

Please replace the paragraph beginning at page 12, line 32, with the following amended paragraph.

Yoked (also called tethered) analogs of human thyrotropin (hTSH) and human chorionic gonadotropin (hCG) have been constructed with the C-terminus of the β subunit fused using a yoking peptide to the N-terminus of the α-subunit. The approach has allowed more extensive structure-function studies and also has resulted in generation of hormones with increased stability and activity. Grossmann et al., showed that the genetic fusion of hTSH α- and β-subunits using

the carboxy-terminal peptide of the hCG β-subunit as a linker created a yoked form of hTSH whose receptor binding and bioactivity were comparable to native hTSH, but had higher thermostability and a longer plasma half-life. The yoked and dimeric hCG expressed in insect cells have been shown to have higher affinity for the LH/CG receptor than native urinary hCG, but are less potent in signal transduction (See Narayan et al., Mol. Endocrinol. 9, 1720 (1995)). The tandem order of subunits - β-subunit-CTP-α-subunit - was chosen based on the studies suggesting the importance of the N-terminal region of hCGβ and C-terminal region of the α-subunit in receptor binding and activation, as described by Ben-Menahem et al., J. Biol. Chem. 276, 29871 (2001) ~~Menahem et al., J. Biol. Chem. 276, 29871 (2001)~~. Fundamentally, this approach also ensures equimolar expression of the subunits and simultaneous affinity labeling of a single recombinant peptide rather than a heterodimer.

Please replace the paragraph beginning at page 16, line 16, with the following amended paragraph.

Synthetic methods may also be used to produce polypeptides and polypeptide subunits of the invention. Such methods are known and have been reported (~~Merrifield, Science, 85:2149 (1963)~~, Olson et al., Peptides, 9, 301, 307 (1988)). The solid phase peptide synthetic method is an established and widely used method, which is described in the following references: Stewart et al., Solid Phase Peptide Synthesis, W. H. Freeman Co., San Francisco (1969); Merrifield, J. Am. Chem. Soc., 85 2149 (1963); Meienhofer in "Hormonal Proteins and Peptides," ed.; C.H. Li, Vol. 2 (Academic Press, 1973), pp. 48-267; Barany and Merrifield, "The Peptides," eds. E. Gross and F. Meienhofer, Vol. 2 (Academic Press, 1980) pp. 3-285 ~~Bavaay and Merrifield, "The Peptides," eds. E. Gross and F. Meienhofer, Vol. 2 (Academic Press, 1980) pp. 3-285~~; and Clark-Lewis et al., Meth. Enzymol., 287, 233 (1997). Polypeptides can be readily purified by fractionation on immunoaffinity or ion-exchange columns; ethanol precipitation; reverse phase HPLC; chromatography on silica or on an anion-exchange resin such as DEAE; chromatofocusing; SDS-PAGE; ammonium sulfate precipitation; gel filtration using, for

example, Sephadex G-75; ligand affinity chromatography, and the like. Polypeptides can also be readily purified through binding of a fusion polypeptide to separation media, followed by cleavage of the fusion polypeptide to release a purified polypeptide. For example, a fusion polypeptide that includes a factor Xa cleavage site between the polypeptide and an affinity tag polypeptide can be created. The fusion polypeptide can be bound to an affinity column to which the affinity tag polypeptide portion of the fusion polypeptide binds. The fusion polypeptide can then be cleaved with factor Xa to release the polypeptide. For example, such a system has been used in conjunction with a factor Xa removal kit using a FLAG affinity tag for purification of the polypeptides of the invention.

Please replace the paragraph beginning at page 26, line 8, with the following amended paragraph.

Antibody fragments of the invention can be prepared by proteolytic hydrolysis of the antibody or by expression in *E. coli* of DNA encoding the fragment. Antibody fragments can be obtained by pepsin or papain digestion of whole antibodies by conventional methods. For example, antibody fragments can be produced by enzymatic cleavage of antibodies with pepsin to provide a 5S fragment denoted F(ab')2. This fragment can be further cleaved using a thiol reducing agent, and optionally a blocking group for the sulfhydryl groups resulting from cleavage of disulfide linkages, to produce 3.5S Fab' monovalent fragments. Alternatively, an enzymatic cleavage using pepsin produces two monovalent Fab' fragments and an Fc fragment directly. These methods are described (U.S. patents No. 4,036,945; 4,331,647; and 6,342,221, and references contained therein; Porter, Biochem. J., 73:119 (1959); ~~Edelman et al., Methods in Enzymology, Vol. 1, page 422 (Academic Press 1967);~~ and Coligan et al. at sections 2.8.1-2.8.10 and 2.10.1-2.10.4).

Please replace the paragraph beginning at page 35, line 15, with the following amended paragraph.

Like other eukaryotic cells, insect cells modify proteins by N-glycosylation. The major processed N-glycan produced by insect cells is usually the paucimannosidic structure, Man3GlcNAc2-N-Asn. The N-glycosylation pathway was extended to insect cells as described in Examples 4 and 5. Genetically transformed insect cells with mammalian β1,4-galactosylatransferase and α2,6-sialyltransferase genes have been described (Hollister et al., Glycobiology v.11, n.1, p.1 (2001) ~~Jasoh et al., Glycobiology v.11, n.1, p.1 (2001)~~). Stably transformed insect cells with β1,4-galactosyltransferase can be used as modified hosts for conventional baculovirus expression vectors to produce mammalianized glycoprotein glycans which more closely resemble those produced by higher eukaryotes. Mimic™ Sf9 Insect Cell line (Invitrogen, Carlsbad, CA), a derivative of the Sf9 insect cell line were modified to stably express a variety of mammalian glycosyltransferases. Typically, insect cells are unable to process N-glycans to the extent that mammalian cells do. The addition of mammalian glycosyltransferases like α2,6-sialyltransferase, β4-galactosyltransferase, N-acetylglucosaminyltransferase I and N-acetylglucosaminyltransferase II to the Mimic™ Sf9 Insect Cells allows for production of biantennary, terminally sialyated N-glycans from insect cells (Hollister, et al., Glycobiology, v. 13, n. 6, p. 487 (2003)).